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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,000	10/04/2005	Hiroko Yanaga	1752-0173PUS1	6374

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EXAMINER
GOUGH, TIFFANY MAUREEN

ART UNIT	PAPER NUMBER
1657	

NOTIFICATION DATE	DELIVERY MODE
07/10/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/552,000	YANAGA, HIROKO	
	Examiner	Art Unit	
	TIFFANY M. GOUGH	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed 2/5/2008 has been received and entered into the case. Claims 1-4 are pending and have been considered on the merits. All arguments and amendments have been considered.

Claim Objections

The previous claim objections have been withdrawn due to applicant's amendment filed 2/5/2008.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 stand rejected under 35 U.S.C. 102(b) as being anticipated by Klein-Nulend et al (Tissue Engineering, vol 4, 1998) supported by Sucheston et al(Ohio J. of Science, 1969).

Applicant claims a method of producing human chondrocytes by co-culturing chondrocytes together with the pericondrium, wherein no non-human animal feeder cells are present in culture. The cartilage tissue from which the chondrocytes are isolated from is preferably auricular cartilage.

Klein-Nulend teach culturing human auricular perichondrium containing chondrocytes, wherein no exogenous feeder cells are present in culture (see Materials and Methods section,p.306 and Results section, p.308-310).

Thus, the reference anticipates the claimed subject matter.

Response to Arguments

Applicant argues that Klein-Nulend disclose differentiation of progenitor cells and that the method of Klein-Nulend does not disclose culturing with chondrocytes.

It is the examiner's position that the perichondrium from ear or rib is disclosed as a convenient source of cells with chondrogenic pontential, i.e. chondrocytes and it is further disclosed that perichondrium cells when transplanted provide a practical source of autologous cells with chondrogenic potential. Although chondrocytes are not literally disclosed, progenitor cells with chondrogenic potential from human perichondrium are disclosed. Also, they disclose that in the explant cultures, chondrocytes were observed (p.308, Results section last paragraph, continued to p. 309). Further, it is known in the art that chondrogenic progenitor cells differentiate into chondrocytes under appropriate conditions as is taught in Applicants Exhibit A, *Histology* reference, p. 132 second paragraph, which states that the perichondrium has two layers…chondrogenic cells which differentiate into chondroblasts. They further teach on p. 133 that chondrocytes are chondroblasts (see underlined section). Also teachings from the *Histology* textbook, including Figure 7-1, further support the Office's position. **To even further support the Office's position is applicant's own arguments, p.17, lines 10-15, wherein applicant states, "...the perichondrium is a membrane tissue surrounding**

cartilage and obtained from the cartilage which provides chondrocytes to be cultured." The chondrocytes are part of the elaborate matrix that is the perichondrium, in addition cartilage grows by adding to the periphery, i.e. appositional growth. Therefore, by practicing a method of culturing perichondrium one would inherently be practicing applicants invention. Further support is also provided by applicant's disclosure, p. 12, Collected cartilage section. Even further, Sucheston teach that the perichondrium, specifically human auricular cartilage, does in fact contain chondrocytes (see p.367, Observations section, Adult cartilage). Thus, without evidence to the contrary and without teachings that the perichondrium was in fact removed from the chondrocytes, by practicing the method of culturing perichondrium to produce chondrocytes, one inherently practices the method as claimed by applicant. Therefore a reference teaching perichondrium with chondrogenic cells does anticipate the claimed subject matter. Further, applicants process recites the language comprises, thus, not limiting their method to the claimed steps.

Claims 1-4 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Van Osch et al (Tissue Engineering, 2000) supported by Sucheston et al(Ohio J. of Science, 1969).

Applicant claims a method of producing human chondrocytes by co-culturing chondrocytes together with the pericondrium, wherein no non-human animal feeder cells are present in culture. The culture is seeded to form a monolayer to give a chondrocyte mass. The cartilage tissue from which the chondrocytes are isolated from is preferably auricular cartilage.

Van Osch et al teach a method of producing chondrocytes by co-culturing perichondrium with chondrocytes. While they do not explicitly state co-culture with chondrocytes, perichondrium is known to possess chondrocytes as is supported by Sucheston who teach that the perichondrium, specifically human auricular cartilage, does in fact contain chondrocytes (see p.367, Observations section, Adult cartilage). Van Osch also disclose that the perichondrium contains chondroprogenitor cells, i.e. thus by practicing the method of culturing perichondrium to produce chondrocytes, one inherently practices the method as claimed by applicant. The perichondrium explants were cultured and grown to form a monolayer (p.322-325).

Response to Arguments

Applicant's arguments filed 2/5/2008 have been fully considered but they are not persuasive.

Applicant argues that the perichondrium does not contain chondrocytes, but chondrogenic cells and that they are distinguishable from one another.

It is the examiner's position that it is not clear according to applicants method and examples how cells of chondrogenic potential are different from chondrocytes. **To even further support the Office's position is applicant's own arguments, p.17, lines 10-15, wherein applicant states, "...the perichondrium is a membrane tissue surrounding cartilage and obtained from the cartilage which provides chondrocytes to be cultured."** As stated above in response to the Klein-Nulend reference it is known in the art that chondrogenic progenitor cells differentiate into chondrocytes under appropriate conditions as is taught in Applicants Exhibit A, *Histology* reference, p. 132 second paragraph, which states that the perichondrium has two layers…chondrogenic cells which differentiate into chondroblasts. They further teach on p. 133 that chondrocytes are chondroblasts (see underlined section). Also teachings from the *Histology* textbook, including Figure 7-1, further support the Office's position. The chondrocytes are part of the elaborate matrix that is the perichondrium, in addition cartilage grows by adding to the periphery, i.e. appositional growth. Therefore, by practicing a method of culturing perichondrium one would inherently be practicing applicants invention. Further support is also provided by applicant's disclosure, p. 12, Collected cartilage section. Applicant also argues that Van Osch teaches that the cartilage itself is useful not the perichondrium, however, according to applicants disclosure, applicant is also collecting cartilage pieces to practice their method, therefore, the argument is not understood. Even further, Sucheston teach that the perichondrium, specifically human auricular cartilage, does in fact contain chondrocytes (see p.367, Observations section, Adult cartilage). Thus, without evidence to the

contrary and without teachings that the perichondrium was in fact removed from the chondrocytes, by practicing the method of culturing perichondrium to produce chondrocytes, one inherently practices the method as claimed by applicant. Therefore a reference teaching perichondrium with chondrogenic cells does anticipate the claimed subject matter. Further, applicants process recites the language comprises, thus, not limiting their method to the claimed steps.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Van Osch et al (Plastic and Reconstructive Surgery, 2001) in view of each of Klein-Nulend et al (Tissue Engineering, vol 4, 1998) and Van Osch et al (Tissue Engineering, 2000) supported by Sucheston et al(Ohio J. of Science, 1969).

Applicant claims a method of producing human chondrocytes by co-culturing chondrocytes together with the pericondrium, wherein no non-human animal feeder cells are present in culture. The cartilage tissue from which the chondrocytes are isolated from is preferably auricular cartilage.

Van Osch (P&R, 2001) teach isolating human auricular cartilage and culturing the isolated chondrocytes in a monolayer for 3-4 passages (see Materials and Methods section, p. 434). The human cells were also seeded into alginate (see Results section, p. 435). No exogenous feeder cells are present in culture.

Van Osch do not teach co-culturing with perichondrium.

Klein-Nulend teach culturing human auricular perichondrium containing chondrocytes, wherein no non-human animal feeder cells are present in culture (see Materials and Methods section,p.306 and Results section, p.308-310). Klein-Nulend teach that the perichondrium from ear or rib is disclosed as a convenient source of cells with chondrogenic pontential, i.e. chondrocytes and it is further disclosed that perichondrium cells when transplanted provide a practical source of autologous cells with chondrogenic potential. The teach that the perichondrium from ear or rib is disclosed as a convenient source of cells with chondrogenic pontential, i.e. chondrocytes and it is further disclosed that perichondrium cells when transplanted provide a practical source of autologous cells with chondrogenic potential. Further, Sucheston teach that the perichondrium, specifically human auricular cartilage, does in fact contain chondrocytes (see p.367, Observations section, Adult cartilage).

Van Osch et al (2000) teach growing cartilage in vitro from auricular perichondrium (p.322). The perichondrium is known to possess and differentiate into chondrocytes and also the ability to generate cartilage (see p.325,328). The perichondrium explants were cultured and grown to form a monolayer (p.322-325).

At the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to co-culture chondrocytes with perichondrium in a method of producing chondrocytes because as Klein-Nulend teach, the perichondrium from ear or rib is disclosed as a convenient source of cells with chondrogenic pontential, i.e. chondrocytes and it is further disclosed that perichondrium cells when transplanted provide a practical source of autologous cells with chondrogenic potential. Further, Van Osch teach that the perichondrium possesses the ability to differentiate into chondrocytes. Thus, it would have been obvious to combine cell/tissue types which are known in the art to be resources of/for chondrocytes.

Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to co-culture chondrocytes with perichondrium with a reasonable expectation for successfully producing chondrocytes because as Klein-Nulend teach, the perichondrium from ear or rib is disclosed as a convenient source of cells with chondrogenic pontential, i.e. chondrocytes and it is further disclosed that perichondrium cells when transplanted provide a practical source of autologous cells with chondrogenic potential. Further, Van Osch teach that the perichondrium possesses the ability to differentiate into chondrocytes. Thus, it would have been motivated to combine cell/tissue types which are known in the art to be resources of/for chondrocytes.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Hiroko et al (WO 02/012451 A1, see English language equivalent Hiroko et al, EP1331264A1) in view of Van Osch et al (Tissue Engineering, 2000) or Klein-Nulend et al (Tissue Engineering, vol 4, 1998) supported by Yi et al (Abstract, J. Korean Soc. Plastic Reconst. Surg., 2001).

Applicant claims a method of producing human chondrocytes, preferably auricular chondrocytes, from cartilage together with the perichondrium comprising growing cells either as a monolayer or multilayer seeding to give a chondrocyte mass.

Hiroko et al (WO 02/012451 A1, see equivalent EP1331264A1) disclose a method of co-culturing human chondrocytes together with perichondrial cells to produce large amounts of human chondrocytes in culture and further multilayer seeding to give to obtain a chondrocyte mass. Hiroko teaches utilization of a cartilage matrix containing collagen and a cartilage therapy material incorporating their chondrocyte mass. The human chondrocytes used in the invention may be any cartilage tissue such as auricular, costal, articular, intervertebral, or tracheal cartilage, especially auricular, costal and articular cartilage (see EP1331246A1 p.3 lines 18-20). Although Hiroko teach the use of feeder cells, specifically non-human animal cells, they do disclose that the feeder cells used contribute to the proliferation and differentiation of the chondrocytes to maintain characteristics of the original cartilage tissue (0017 and 0018). They further teach that no feeder cells have been known for human chondrocytes.

As stated above, Van Osch et al teach a method of producing chondrocytes by co-culturing perichondrium with chondrocytes. The perichondrium explants were cultured and grown to form a monolayer (p.322-325).

Klein-Nulend teach culturing human auricular perichondrium containing chondrocytes, wherein no non-human animal feeder cells are present in culture (see Materials and Methods section,p.306 and Results section, p.308-310). Klein-Nulend teach that the perichondrium from ear or rib is disclosed as a convenient source of cells with chondrogenic pontential, i.e. chondrocytes and it is further disclosed that perichondrium cells when transplanted provide a practical source of autologous cells with chondrogenic potential. The teach that the perichondrium from ear or rib is disclosed as a convenient source of cells with chondrogenic pontential, i.e. chondrocytes and it is further disclosed that perichondrium cells when transplanted provide a practical source of autologous cells with chondrogenic potential. Further, Sucheston teach that the perichondrium, specifically human auricular cartilage, does in fact contain chondrocytes (see p.367, Observations section, Adult cartilage).

Yi et al teach that the perichondrium is a new source of cartilage for auricular cartilage grafts. They teach grafts wherein the perichondrium is preserved and further suggest the perichondrium to produce chondrogenic cells and serves as a scaffold for cartilage differentiation.

At the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to have co-cultured chondroctyes together with the perichondrium because while Hiroko disclose that the feeder cells used contribute to the proliferation and differentiation of the chondrocytes to maintain characteristics of the original cartilage tissue (0017 and 0018), they further teach that no feeder cells have been known for human chondrocytes. Thus, there is a need for “feeder cells” for human chondrocytes. Therefore, given what is known in the art of the proliferative and differentiation abilities of the perichondrium, its ability to generate and maintain characteristics of cartilage, and it’s chondrogenic potential as taught by Van Osch and Klein-Nulend further supported by Yi et al, one would have been motivated to co-culture chondrocytes with it’s perichondrium intact.

Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to have co-cultured chondrocytes with its perichondrium with a reasonable expectation for successfully producing human chondrocytes because there is a need in the art for cells/tissues which are capable of supporting the proliferation and differentiation of chondrocytes. Given the ability of the perichondrium to do so as is taught by Van Osch and Klein-Nulend further supported by Yi et al, one would have expected success in co-culturing chondrocytes with its intact perichondrium.

Response to Arguments

Applicant's arguments filed 2/5/2008 have been fully considered but they are not persuasive.

Applicant argues that the perichondrial cells in the chondrogenic stage are distinguishable from the perichondrium, yet do not elaborate as to how they are different. Thus, the argument is not persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). To be fully responsive, the above response to each of applicants arguments against the references individually apply hereto.

Conclusion

NO claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIFFANY M. GOUGH whose telephone number is (571)272-0697. The examiner can normally be reached on M-F 8-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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